

## REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 5 and 6 were pending in this application when last examined.

Claim 5 is amended to clarify the claimed invention. This is supported by the specification from page 6, line 26 to page 7, line 19 which describes that the simultaneous expression of the normal subunit and the mutant subunit is more appropriate for a model animal representing human epilepsy. In addition, “PDGF- $\beta$  chain promoter” is defined in the amended claim 5. This is an answer to the Examiner’s question on page 6, second paragraph of the Office Action. No new matter is added.

On pages 2-7 of the Office Action, claims 5 and 6 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Matsuhima et al. (2002, Epilepsy Research 48:181-186) in view of McColl et al. (2003, Neuropharmacology 44:234-243).

Applicants respectfully traverse this rejection.

In the amended claim 5, it is specified that the transgenic rat has a mutated CHR $\alpha$ 4 transgene, together with a normal (endogenous) CHR $\alpha$ 4 gene. The specification from page 6, line 26 to page 7, line 19 describes that the simultaneous expression of the normal subunit (i.e., the normal CHR $\alpha$ 4) and the mutant subunit (i.e., the mutant CHR $\alpha$ 4) is more appropriate for a model animal presenting human epileptic seizure.

In contrast to the Examiner’s position, McColl studied “knockout mice” to investigate extreme hypofunction of CHR $\alpha$ 4, but not “transgenic mice” established by introducing a mutant CHR $\alpha$ 4 gene (Abstract). McColl describes that the knockout mice did have spontaneous seizure, but following administration of PTZ, a GABA antagonist, the mice had a greater number of generalized clonic seizure. McColl concluded that intact CHR $\alpha$ 4 subunits provide significant in vivo protection against the proconvulsant effects of GABA antagonism (Abstract). Therefore, McColl teaches that hypofunction of CHR $\alpha$ 4 leads to occurring of epileptic seizure due to GABA antagonism, and intact CHR $\alpha$ 4 is important for protection against the induced epileptic seizure.

On the contrary, the transgenic rat of the claimed invention has both intact CHR $\alpha$ 4 and mutant CHR $\alpha$ 4, and can develop a spontaneous epileptic seizure during sleep. The significance of intact (normal) CHR $\alpha$ 4 in a model animal presenting human epileptic seizure is

not taught or suggested by McColl. In fact, as noted above, McColl suggests that intact CHRNA4 would protect against seizure.

Thus, Applicants respectfully note that the cited references fail to teach or suggest the claimed transgenic rat which can develop spontaneous epileptic seizures during sleep.

Applicants further note that these claimed amendments were previously considered by the Examiner in a facsimile of November 28, 2011. The Examiner noted by telephone that such limitations should put this case in condition for allowance.

Thus, for the above noted reasons, this rejection is untenable and should be withdrawn.

### **CONCLUSION**

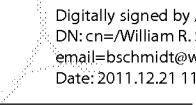
In view of the foregoing amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notice to that effect is hereby requested.

If the Examiner has any comments or proposals for expediting prosecution, please contact the undersigned attorney at the telephone number below.

Respectfully submitted,

Shinichi HIROSE et al.

/William R.  
By Schmidt, II/

  
Digitally signed by /William R. Schmidt, II/  
DN: cn=/William R. Schmidt, II/, o, ou,  
email=bschmidt@wenderoth.com, c=US  
Date: 2011.12.21 11:33:51 -05'00'

William R. Schmidt, II  
Registration No. 58,327  
Attorney for Applicants

WRS/srp  
Washington, D.C. 20005-1503  
Telephone (202) 721-8200  
Facsimile (202) 721-8250  
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